



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Tetramethrin; Bridging Data with Neo-Pynamin Forte
Submitted in Support of Neo-Pynamin (Tetramethrin)
Guideline Study 83-4 for Reregistration

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ACTION REQUESTED: Review submitted studies with neo-pynamin forte to determine whether they support the 2-generation rat reproduction study with neo-pynamin forte as a satisfactory study for the 83-4 Guideline requirement for neo-pynamin.

BACKGROUND: Neo-Pynamin (tetramethrin) is a racemic mixture of four stereoisomers, the cis and trans isomers of two optical enantiomers. The four stereoisomers, (1R,trans), (1R,cis), (1S,trans), and (1S,cis) are present in technical neo-pynamin in a ratio of 4:1:4:1.

Neo-Pynamin Forte consists of cis and trans isomers in a 1:4 ratio of only the R isomer. Therefore, the mixture consists of (1R,trans) and (1R,cis) isomers in an approximately 4:1 ratio.

The (1R,trans) isomer is biologically more active than the other isomers. Previously reviewed reproduction studies include both a 1-generation rat reproduction study with neo-pynamin and a 2-generation rat reproduction study with neo-pynamin forte. In the neopynamin study, the NOEL was 1000 ppm and the LEL was 3000 ppm due to decreased pup body weights during lactation. The doses were 0, 1000, 3000, and 6000 ppm in Sprague-Dawley rats. In the 2-generation rat reproduction study with neo-pynamin forte, the NOEL was 500 ppm and the LEL was 3000 ppm (HDT) due to decreased pup body weight of F1 and F2 litters, decreased parental body weight, and bile duct hyperplasia of the liver in F1 females. Doses were 0, 100, 500, and 3000 ppm in Sprague-Dawley rats.

During the FIFRA '88 Reregistration process, HED requested that bridging data be submitted with neo-pynamin forte to demonstrate that the 2-generation rat reproduction study with neo-pynamin forte is acceptable in fulfilling the data requirement for a reproduction study for reregistration of neo-pynamin. The bridging data are reviewed in this memorandum.

CONCLUSIONS: With the exception of some acute data, the reviewed toxicology studies with neo-pynamin forte submitted as bridging data were only acceptable as core-supplementary data. However, the results indicate that the 2-generation rat reproduction study with neo-pynamin forte, previously reviewed and accepted as core-minimum data, is acceptable in fulfilling the rat reproduction study, 83-4, data requirement for the reregistration of neo-pynamin (tetramethrin).

Additionally, it can be concluded that both neo-pynamin (the 1RS, racemic mixture) and neo-pynamin forte (1R, cis/trans mixture) behave essentially the same as far as their metabolic interactions are concerned. Elimination from the body is essentially complete within 7 days after administration, with about equal amounts being present in the urine and feces. Residues in tissues are very low. The major metabolic reactions are similar between the cis and trans isomers and involve cleavage of the ester linkage, loss of the hydroxymethyl group from the alcohol, oxidation, conjugation and excretion mainly as glucuronides.

A direct comparison of the data base for neo-pynamin forte and neo-pynamin can only include the acute and reproduction studies. Although there are additional studies for both neo-pynamin forte and neo-pynamin, the routes of administration, duration of the studies, and animal species were so different that these other studies were not considered as useful bridging data. The following bridging data were used:

NEO-PYNAMIN

Rat-Acute Dermal (AD) >5000 mg/kg

NEO-PYNAMIN FORTE

Rat-AD >5000 mg/kg

2

Rat-Acute Oral (AO) >5000 mg/kg
Mouse-AO = 2000 mg/kg
Repro. NOEL= 1000 ppm

Rat-AO >5000 mg/kg
Mouse-AO = 1000 mg/kg
Repro. NOEL= 500 ppm

Based on the acute and reproduction studies with both compounds, neo-pynamin forte is at least twice as toxic as neo-pynamin. DER's for the neo-pynamin forte studies are attached.